bination of norgestrel and ethinyl estradiol (Ovral, 2 tablets) within 72 hours, followed by two more tablets 12 hours later. Other levonorgestrel- and norgestrel-containing pills may be substituted if the dosage is adjusted (Table 1). Over-the-counter antiemetics help control side effects.

Single-cycle pregnancy rates with emergency contraception are reduced to 2%, which represents a 75% reduction in pregnancy risk. There is now a toll-free emergency contraception hotline operated by the Office of Population Research at Princeton University for patients and professionals. This number is (800) 584-9911 for information about providers of emergency contraception.

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Managing Viral Exposure During Pregnancy

THE MANAGEMENT OF viral exposure and disease during pregnancy presents many unique challenges because of possible effects on both a woman and her developing fetus. Maternal rubella infection is a classic example of this. In 1984, before the use of the rubella vaccine, a major epidemic of rubella infection occurred in the United States. During that year, about 20,000 new cases of the congenital rubella syndrome and 11,000 pregnancy losses due to rubella infection occurred in the United States. Certain viruses, such as varicella, may also cause more severe maternal disease during pregnancy. Varicella pneumonia is a relatively common, potentially life-threatening complication of varicella infection during pregnancy.

For most viral diseases, the diagnosis in a pregnant woman rests on serologic testing. Many women with proven viral infection report few, if any, symptoms of infection. Diagnosis is made by demonstrating viral-specific immunoglobulin (Ig) M or a fourfold titer change in specific IgG levels. Routine serologic testing in the United States is currently recommended only for rubella, and if the woman is seronegative, vaccination is recommended after delivery.

As mentioned, varicella infection in pregnancy can cause severe maternal pneumonia in 5% to 10% of cases. Because of this, varicella zoster immune globulin (VZIG) should be given to all nonimmune pregnant women within 72 hours of exposure to varicella. Serologic testing should be done before VZIG is given because as many as 90% of women are immune. The effect of VZIG administration on fetal infection is unknown. Fetal disease—limb hypoplasia, cicatricial skin lesions, retardation, or cortical atrophy—occurs in less than 2% of fetuses. Maternal infection less than five days before delivery also causes neonatal infection due to the lack of time for the development of maternal protective IgG antibodies.

Parvovirus infection in pregnancy is one of the few treatable fetal conditions. The diagnosis in a pregnant woman is most commonly made after the discovery of nonimmune hydrops in her fetus. The diagnosis is confirmed either by maternal serologic testing or identification of the virus in amniotic fluid specimens by polymerase chain reaction (PCR). Parvovirus can cause bone marrow failure in the fetus, with fetal death occurring in as many as 5% of maternal infections. The hydrops resulting from this aplastic crisis has been successfully treated with the intrauterine transfusion of erythrocytes. In some cases, hydrops has resolved spontaneously. The current recommendation is for serial ultrasonograms to be done for as long as 16 weeks following maternal disease to monitor for the development of hydrops.

Cytomegalovirus is the most common cause of congenital viral infection. An estimated 0.2% to 2.2% of neonates are infected in utero, with 5% to 10% being symptomatic at birth. Fetal infection can occur with both primary and recurrent maternal infection; the likelihood of severe infection is much higher with primary infection, and early infection is associated with much more severe disease. Overall, fetal infection occurs in about 40% of cases of primary maternal infection. Although only 10% of infected infants are symptomatic at birth, symptoms, most commonly sensorineural hearing loss, will develop in an additional 5% to 10% by 2 years of age. Fetal infection in utero can be diagnosed by the culture of cytomegalovirus in the amniotic fluid or by PCR of amniotic fluid. The sensitivity of these two approaches is currently unclear.

Perhaps the virus with the greatest public health policy implication is the human immunodeficiency virus (HIV). The Centers for Disease Control and Prevention has reported that as of 1991, about 7,000 infants would be born each year to HIV-infected mothers and, of these, 1,000 to 2,000 would be infected. Because of this, a trial was begun in 1991 of maternal zidovudine therapy during pregnancy to prevent vertical transmission. Preliminary analysis of data from this trial has indicated a 67.5% reduction in the risk of HIV transmission. These results have led to the controversial recommendation that all women be screened for HIV during pregnancy and treated with zidovudine if infected.

What does the future hold for the diagnosis and management of viral diseases during pregnancy? An important advance will be the application of PCR-based diagnoses in fetuses. In this way, we will be able to more accurately identify affected fetuses. Also, new antiviral agents, if found safe for fetuses, may help decrease vertical disease transmission rates or actually treat fetuses in utero.

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Assisted Reproductive Technologies

ACCORDING TO THE MOST recent statistics published by the American Society for Reproductive Medicine, a total of 39,390 cycles of assisted reproductive technologies were initiated in the United States during 1994. A total of 9,573 deliveries occurred as a result of these technologies. Because of these high success rates, assisted reproductive technologies are increasingly being offered to infertile couples with a variety of diagnoses. Nevertheless, the most appropriate candidates for these technologies are those in whom other, more conventional treatments have failed. Patients with unexplained infertility are usually offered several cycles of superovulation and intrauterine insemination before proceeding to assisted reproductive technologies. Patients with pelvic factor infertility are appropriate candidates for in vitro fertilization (IVF), either after a failed tuboplasty or, if tubal disease is severe, in place of a pelvic reconstructive operation. Hydrosalpinges, however, should be either removed or opened by a cuff neosalpingostomy to drain the hydrosalpinx before IVF. Couples whose infertility is due to a male factor—for example, the husband's sperm have decreased fertilizing potential—are also appropriate candidates for IVF and, if the semen analysis is markedly abnormal, may benefit from micromanipulation of the gametes

To enhance success, most assisted reproductive programs use controlled ovarian hyperstimulation before the collection of gametes. The most commonly used regimen includes pretreatment with a gonadotropin-releasing hormone agonist and subsequent stimulation with human menopausal gonadotropins (hMG). The recombinant form of follicle-stimulating hormone will be introduced in the United States in 1997, and its use will most likely replace that of hMG in the same way that recombinant insulin has replaced other preparations. Natural-cycle (or "unstimulated") IVF, which depends on the selection of a single dominant follicle by the patient's own reproductive axis, continues to occupy a small niche within the assisted reproductive technologies. Whereas unstimulated cycles are easier to do, cheaper, and spare the endometrium the adverse effects of controlled ovarian hyperstimulation, the success rate of natural-cycle IVF is consistently lower than that of stimulated cycles. It appears that two cycles of natural-cycle IVF are required to achieve the success of a single stimulated cycle.

A key element of the assisted reproductive technologies is the collection of the oocytes. The transvaginal ultrasound-directed follicle-aspiration method is now standard. It can be achieved outside of an operating room with conscious sedation. The gamete intrafallopian transfer (GIFT) procedure, which involves placing gametes into the fallopian tubes, still requires general anesthesia and an operating room for the laparoscopy. As microlaparoscopic techniques become more commonplace, conscious sedation may also be used for the GIFT procedure.

Oocyte donation, a logical consequence of oocyte collection, has also grown substantially. This is due to the unanticipated finding that oocyte quality is a major determining factor of the success of the assisted reproductive technologies. Therefore, women with reduced oocyte quality, diminished ovarian reserve, and those older than 40 benefit substantially from the donation of oocytes from younger women. According to the most recent statistics, 3,119 donor oocyte cycles were initiated in the United States during 1994 with an overall success of 46.8% deliveries per retrieval. The technique of oocyte donation presents a unique physiologic configuration, as the oocytes are retrieved from one woman and are donated to another woman. Therefore, both ovarian stimulation and endometrial preparation can be controlled independently. For this reason, success rates of oocyte donation are consistently the highest of all the assisted reproductive technologies. No decline in success rates has been observed with increasing age of the recipient. Therefore, it appears that whereas the ovary ages, uterine receptivity does not decline, even for recipients well into their sixth decade of life. Regardless of the source of oocytes, the trophoblast and fetus are always immunologically distinct from the mother. Therefore, oocyte donation presents no additional difficulties with "rejection."

Whether or not success rates of the assisted reproductive technologies have already been maximized is not yet clear. Each year still seems to bring higher success rates on an individual clinic basis, as well as the overall statistics for the country as a whole. An additional benefit of these technologies is that success rates do not appear to decline over successive cycles. Therefore, they can be repeated for as many as three to six cycles to achieve high cumulative pregnancy rates. In most cases, the limiting step in the overall success of these procedures is the cost. The cost per cycle ranges from about $6,000 to $15,000, depending on the clinic, the type of technology (laparoscopy adds substantial cost), other interventions (intracytoplasmic sperm injection or embro freezing), and the amount of gonadotropins required to achieve stimulation. Whereas many states have mandated the coverage of assisted reproductive technologies, most insurance companies in California still do not cover this service. The national trend, however, is toward increased coverage of infertility treatment, including a certain number of cycles (usually 3) of treatment. Therefore, the future of these technologies appears headed toward technologic advancement, increased cost-effectiveness, and greater availability.

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